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Bozinov, O

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Modern Intraoperative Ultrasound in Neurosurgery – Improving Orientation and Resolution

Zur Erlangung der Venia Legendi der Universität Zürich

Dr. med. Oliver Bozinov

Oberarzt an der Klinik für Neurochirurgie des UniversitätsSpital Zürich

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Summary

The treatment or resection of any lesion in the brain and loss of cerebral spinal fluid (CSF) leads to intraoperative brain shift. Therefore, commonly used neuronavigation systems based on preoperative data lose their accuracy [Bonsanto 2001]. The search for improved accuracy has led to recent developments in a variety of intraoperative imaging modalities such as intraoperative MRI and computer tomography (CT) or other new concepts [Bernays 2003, Black et al. 1997, Nakato et al. 2003, Nimsky et al. 2000, Stummer et al. 2006]. Significant improvements in ultrasound image quality over the past decade and the fact that probes have become small enough to fit into a minimally invasive craniotomy have led to a continued use of intraoperative ultrasound. Nevertheless orientation and resolution are frequently mentioned for reserved use of this cost effective intraoperative imaging modality. The connection of ultrasound and navigation systems led to improvements in orientation [Unsgaard et al. 2002, Tronnier et al. 2001] and further developments have enhanced the intraoperative possibilities and intraoperative ultrasound remained as an alternative intraoperative imaging modality.

Once the ultrasound probe is tracked and plain images are transferred as well as integrated into the navigation system, further ultrasound tools/abilities can be added to the neuronavigation. In **Article 1** we describe the intraoperative landmarking of vascular anatomy by integration of duplex and Doppler ultrasound in image-guided surgery. The image-guided visualization of the intralesional blood flow could additionally aid further understanding of the anatomy of the nidus and the anatomic relation of its feeding and draining vessels in vascular surgery, particularly during complex AVM surgery.

The problem of brain shift is significant in cystic lesions after puncture and preoperative data sets of MRI/CT may loose this value. In **Article 2** we analyzed the image-guided ultrasound for recurrent cystic gliomas. The connection of neuronavigation and ultrasound helped us to estimate the brain shift when comparing both imaging modalities next to each other or in an overlay method. According to our results, the tumor resection should be guided mainly by ultrasound after dura opening or cyst drainage rather than by neuronavigation.

After significant improvement of orientation through combination of intraoperative ultrasound and neuronavigation (here now in a one platform setting), we retrospectively reviewed in **Article 3** the potential benefit of image guided ultrasound in neurosurgical routine. The orientation of navigated duplex sonography was faster and better to understand compared to

non-navigated duplex sonography and therefore demonstrated advantages over conventional intraoperative ultrasound.

Intraoperative ultrasound in neurosurgical spinal lesions is a very common aid and is basically without any alternatives. With technical advances (smaller probes and higher frequency ranges) this intraoperative imaging technique can even enhance its value. In **Article 4** we retrospectively studied a series of spinal tumor patients and the role of intraoperative ultrasound assistance. Guidance of myelotomy was an important factor in this study and high-frequency linear probes improved the latter significantly.

In **Article 5** we further elaborate this topic by focusing on a special intramedullary vascular lesion ("spinal cavernous malformation") in a recently published case series, where myelotomy plays a key role. With further improvement of the linear probe (up to 15 MHz) resection control was monitored and real time 3D ultrasound was introduced into spinal intradural surgery. We showed that the resection control was dependent on the chronic or acute situation of the complex vascular lesion. Active spinal cavernous malformations with edema or hemorrhage were more difficult to interpretate than inactive lesions.

The novel available intraoperative real time 3D ultrasound was initially tested in a small series of intracranial cavernomas and published in **Article 6**. The new concept behind true real time 3D imaging is that the array probe allows the rendering of full volume data and no acquisition procedure is necessary. The orientation improved through simultaneous display of two image planes but resolution remained fair for deep seated cavernomas.

In **Article 7** we investigated the impact of intraoperative real time 3D ultrasound in a case series of pediatric tumor patients and achieved similar gross total resection rates compared to series with intraoperative MRI. Especially the removal of cystic tumors may be facilitated by this intraoperative imaging modality due to fast orientation after significant brain shift.

The advance of intraoperative 3D ultrasound in Neurosurgery have been summarized in **Article 8** dealing with the advantages and limitations of its use. Navigated 3D ultrasound improves orientation significantly but requires acquisition time and offers only retrospective view. Real time 3D imaging delivers live imaging but not in the familiar planes as the navigation system. The orientation improved compared to 2D solutions, but the resolution did not increase. A combination of real time 3D ultrasound and neuronavigation would be the optimal intraoperative imaging tool if detailed resolution will further increase.

All presented articles have contributed to easier or more sophisticated use of intraoperative ultrasound by technical advances (3 articles). This was confirmed by good neurological outcome and resection control (5 articles) in its competitive clinical use.

Article 1: Intraoperative landmarking of vascular anatomy by integration of duplex and Doppler ultrasound in image-guided surgery. Technical note. Sure U, Benes L, **Bozinov O**, Woydt M, Tirakotai W, Bertalanffy H. Surg Neurol 2005 63:133-41

Article 2: Image-guided ultrasound for recurrent cystic gliomas. **Bozinov O***, Enchev Y*, Miller D, Tirakotai W, Heinze S, Benes L, Bertalanffy H, Sure U. Acta Neurochir 2006 148:1053-63; *contributed equally

Article 3: Is the image guidance of ultrasound beneficial for neurosurgical routine? Miller D, Heinze S, Tirakotai W, **Bozinov O**, Sürücü O, Benes L, Bertalanffy H, Sure U. Surg Neurol 2007 67:579-87

Article 4: Intraoperative ultrasound assistance in treatment of intradural spinal tumors. Zhou H, Miller D, Schulte DM, Benes L, **Bozinov O**, Sure U, Bertalanffy H. Clin Neurol Neurosurg 2011 113:531-7

Article 5: Intra-operative high frequency ultrasound improves surgery of intramedullary cavernous malformations **Bozinov O**, Burkhardt JK, Woernle C, Hagel V, Ulrich NH, Krayenbühl N, Bertalanffy H. Neurosurg Rev 2011 Nov 12 [Epub ahead of print]

Article 6: Intraoperative localization of intracranial cavernomas by real time 3D ultrasound: First experiences (Technical Note) Aboulfetouh I, Ulrich NH, **Bozinov O**, Bertalanffy H. Pan Arab Journal of Neurosurgery 2010 14:81-85 (No Pubmed listing)

Article 7: Resection of pediatric intracerebral tumors with the aid of intra-operative real-time 3-D ultrasound. Ulrich NH, Burkhardt JK, Serra C, Bernays R, **Bozinov O**. Childs Nervous System 2011 Sep 17 [Epub ahead of print]

Article 8: Advantages and limitations of intraoperative 3D ultrasound in neurosurgery. Technical note. **Bozinov O**, Burkhardt JK, Fischer CM, Kockro RA, Bernays RL, Bertalanffy H. Acta Neurochir Supp 2011 109:191-6

Introduction

Implantation of intraoperative imaging in Neurosurgery

Optimal intraoperative imaging is a general dream of any Neurosurgeon. It is very inconvenient to find out with postoperative imaging, that the tumor has been missed, the clip position of aneurysms is inadequate or occludes unintentionally important structures, the wrong spinal level has been opened or simply the residual tumor is significantly too large and could have been further reduced without any danger. Therefore, all postoperative imaging techniques, such as angiography, MRI, CT, X-Ray or ultrasound, have been aimed to be installed intraoperatively [Bernays 2003, Black et al. 1997, Nakao et al. 2003, Nimsky et al. 2000, Raabe et al. 2005, Schaller et al. 2011, Schlagenhauff et al. 1972, Steinmeier et al. 1998].

Frameless image-guided systems were introduced into clinical practice at the end of the last century to have preoperatively acquired images available during Neurosurgical procedures. They became a standard adjunct to neurosurgical tumor resection procedures and offer a full complement of navigational information including localization, orientation and guidance [Barnett 1999]. However, navigation techniques, which are based on preoperative data, are of limited intraoperative value, because of their inability to account for changes that occur during surgery due to brain shift [Doward et al. 1998]. Benefits of intraoperative MRI and CT techniques have been pointed out by numerous papers [Bernays 2003, Nakao et al. 2003, Nimsky et al. 2000 and 2001]. Intraoperative CT has not become a popular solution, because of ionizing radiation and image artifacts, as well as the limited tumor definition [Bernays 2003]. When using intraoperative MRI, a prolonged image acquisition procedure, high costs, special surgical equipment and the limited working space have to be considered; therefore neurosonography has further developed as a possible alternative to intraoperative MRI [Bernays 2003, Joedicke et al. 1998, Tronnier et al. 2001, Unsgaard et al. 2002].

Surgical relevance for ultrasound

Intraoperative ultrasound conducts true real-time imaging for significanty lower equipment costs than MRI or CT. This simple technical tool provides intraoperative real-time localization of a lesion. Common neurosurgical lesions have a different echogenicity than the normal brain and therefore ultrasound can provide intraoperative imaging of the lesion [van Velthoven et al. 2003]. It defines borders and allows detection of residual tumor as well as differentiation of the tumor from cysts. Initial complaints about poor spatial and contrast resolution have been disproven by recent technological advances, especially with high-end ultrasound probes and reduction of probe sizes. Although a certain learning curve is still needed for the interpretation of intraoperative ultrasound images, novel developments in combination with neuronavigation have demonstrated feasibility even for neurosonoraphic unexperienced Neurosurgeons [Miller et al. 2007, Tirakotai et al. 2006]. Le Roux et al. [1992] described a possible enhancement of operative delineation and extent of resection for low-grade gliomas. These findings were followed by numerous surgeons and also by our group [Barnett 1999, Tronnier et al. 2001, Enchev et al. 2006]. The combination of navigation and intraoperative US had a significantly better agreement with histopathology compared to navigated MRI T1 for low-grade astrocytomas [Unsgaard et al. 2002]. Also high-grade gliomas have a significant uptake in echogenicity and therefore resection can be guided by ultrasound. The benefit of a gross total resection (GTR) is well known and for instances fluorescence resections of contrast-enhancing tumor leads to improved progression-free survival in patients with glioblastoma [Stummer et al. 2006]. Another favorable group of lesions for ultrasound guided resection are cavernomas. Their significant hyperechogenicity relies most likely on the concentrated hemoglobin in the lesion, as seen on hemorrhages in ultrasound images [Aboulfetouh et al. 2010, Bozinov et al. 2011, Dammann et al. 2011, Miller et al. 2011]. Vessels close to the cavernoma, like the often-associated developmental venous anomaly, are of particular interest for the surgeon and can be visualized by duplex and Doppler ultrasound [Sure et al. 2005].

In order to facilitate optimal ultrasound imaging, nearly all patients must be positioned (during surgery) with a near vertical channel of the craniotomy. By such positioning saline would remain in the resection cavity after dura opening for further ultrasound imaging. Air bubbles could limit image acquisition by disturbing acoustic shadows [Unsgaard 2006]. This technique needs to be used to facilitate sonographic resection control. It is important to mention, that in all cases, the craniotomy should not be enlarged merely for the use of ultrasound probes.

Basically two technical directions have significantly improved the usage of intraoperative ultrasound in Neurosurgery. The first one is the combination of ultrasound and neuronavigation. The second one is technical improvement, including smaller assembling of the probes as well as innovative new real time 3D ultrasound. The following 3 chapters and articles from our group represent these technical developments accompanied with these new abilities and the clinical use as well as their clinical impact.

Ultrasound and Neuronavigation

Article 1: **Intraoperative landmarking of vascular anatomy by integration of duplex and Doppler ultrasound in image-guided surgery. Technical note.**

Our group in Marburg has gained significant experience with the combined use of neuronavigation in stereotactic and endoscopic procedures [Tirakotai et al. 2004 (a) and 2004 (b)]. Integration of intraoperative ultrasound into a neuronavigation system has started in the beginning of the last decade and we connected our existing high end ultrasound machine (Toshiba, Powervision 6000 SSA-370A, Tokyo, Japan) with a probe that can be sterilized to the neuronavigation system (VectorVision2, BrainLab, Heimstetten, Germany). This technical note relays on a case series of 47 surgical procedures performed by the first author who initiated these studies. The navigated ultrasound image could be visualized on the navigation screen. We developed a technique that enables online image overlay and guidance of intraoperative ultrasound images in both Doppler and duplex (color mode and B-mode) mode with data derived from preoperative MRI or CT. Our interest was directed to the intraoperative vessel anatomy. During AVM surgery, the landmarking of vessels helped in the visualization and navigation of deep-feeding or draining vessels (Fig. 1).

Figure 1: Intraoperative screenshot during surgery on a frontal AVM. The duplex color demonstrates the flow inside the feeder (white arrow). The arterial origin of this vessel is confirmed by an acoustic Doppler control (white arrow). Lower right, The screenshot shows the reconstructed MRI plane according to the ultrasound plane (upper left). Landmarking of the feeder has already been performed according to the ultrasound data. Note the red circled dots highlighting the feeder. Lower left, Image composition of the upper left and lower right images.

Our "2-platform solution" consisted of a high-end external ultrasound system, which was integrated into an existing neuronavigation platform (independent neuronavigation and ultrasound systems). Its correct use required a considerable amount of experience in both standard neuronavigation techniques and ultrasound. Such an advanced image-guided technique needed an experienced user. The integration of ultrasound into the neuronavigation platform had to be performed by the calibration of the ultrasound probe. This had to be completed either during or before surgery. One further limitation of this technical combination was the so called fusion of the images, which was more or less an overlay, then a fusion. This technique is limited by the fact that the fusion of the ultrasound image with the preoperative data is only correct at the beginning of the surgery, but not necessarily for the overlayed images after brain shift (due to CSF loss after dura opening). However, the fusion was highly accurate before CSF was released.

In this study we demonstrated that both image-guided ultrasound and duplex-guided integration of vascular anatomy into the neuronavigational data set were technically possible. The image-guided visualization of the intralesional blood flow could additionally aid further understanding of the anatomy of the nidus and the anatomic relation of its feeding and draining vessels, particularly during complex AVM surgery. Furthermore, postresectional control of the image-guided ultrasound helped in the determination of small sections of residual nidus at the end of surgery.

Article 2: Image-guided ultrasound for recurrent cystic gliomas.

Two-platform solutions consist of complex pre- and postoperative arrangements, such as calibration and technical connections. In cooperation with Brainlab our group developed an one-platform setup [Tirakotai et al. 2006]. This device was a "plug and play" solution. The precalibrated tracked ultrasound probe IGSonic 10V5 (5–7.5MHz frequency, with max. 120mm depth at 5MHz) was just connected via one cable to the neuronavigation and could be used immediately. The images were integrated in the navigation setup and therfore overlay of both images (MRI/CT and ultrasound) were immediately possible intraoperatively. We used this new development in a first case series of cystic gliomas and these user friendly images were easy to understand even for neurosurgeons without major experience in intra-operative ultrasound.

This integrated intra-operative ultrasound modality was handy and afforded true real-time imaging, which was valuable for evaluating the precise tumor location and the anatomical relationship between the tumor and surrounding structures such as vessels and ventricles. Particularly, the ultrasound image displayed in a green scale on the composite overlay was judged to be very helpful in distinguishing between the image information (MRI and ultrasound) (Fig. 2). The intra-operative landmarking of the vascular anatomy by integrating duplex and Doppler ultrasound as previously described was advantageous during the resection of recurrent gliomas, especially when gliomas covered or dislocated neighboring vessels.

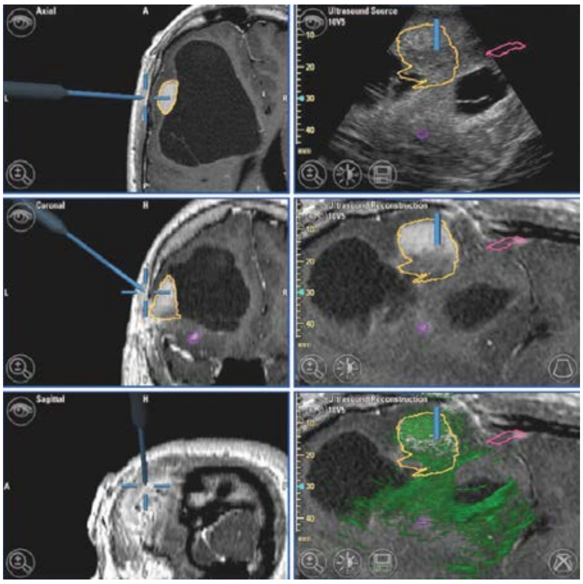


Figure 2: Intra-operative screenshot during surgery for a left frontal recurrent cystic astrocytoma. Left side (upper, centre, lower): Axial, coronal and sagittal MRI views. Right side: The ultrasound image (upper), its corresponding reconstructed MRI plane (centre) and its corresponding reconstructed MRI plane with the superimposed semi-transparent green overlay image (lower), which offers a good visualization of the hyperechogenic tumor in a composite (ultrasound and MRI) image, are displayed. Preoperatively, the tumor has been outlined (yellow) in the MRI data set and is superimposed onto the ultrasound image (upper right).

One of the main problems with cystic lesions and navigation is the immediate brain shift once a cyst is punctured. Preoperative images for neuronavigation cannot be used anymore without caution. Intraoperative ultrasound in these cases and connection to the neuronavigation helped to estimate the brain shift when comparing both imaging modalities next to each other or in an overlay method. According to that, the tumor resection should be guided mainly by ultrasound after dura opening then by neuronavigation. The integrated ultrasound probe from the company BrainLab (IGSonic), however, did not represent a high-end and high frequency probe, but more a compromise in all necessary neurosurgical fields to keep the development and selling costs low. The resolution was only in a medium range. There were significant advantages in orientation, but resection control with this lower frequency ultrasound probe was therefore limited.

Unsgaard et al. [2006] published a benchmark review article regarding developments in reconstructed 3-D US. The authors used the intra-operative imaging system SonoWand®

(Mison, Trontheim, Norway) that is a high-end ultrasound platform with a supplementary navigation system. Several groups (including ours) have shown that the combination of image-guided neurosurgery with 3-D ultrasound increases the diagnostic value significantly [Unsgaard et al. 2006, Enchev et al. 2006, Lindner et al. 2006]. Furthermore, Letteboer et al. [2005] demonstrated that immediate updating during the operation helps to minimize the problem of brain shift.

Article 3: Is the image guidance of ultrasound beneficial for neurosurgical routine?

Ultrasound users without neuronavigation experiences need anatomical landmarks, such as ventricles, falx, tentorium or bone to get orientation in the intraoperative anatomical field. Connection of the neuronavigation and especially in an one-platform solution added a very easy to use ultrasound with its corresponding preoperative MRI/CT image in the same oblique plane. Either these two imaging modalities were presented next to each other or in an overlay display. In this situation anatomical landmarks are not as necessary as with ultrasound use alone. Ultrasound beginners will therefore benefit from this connection.

In this case series 29 patients with intracranial tumors were operated with the aid of intraoperative ultrasound. Image-guided sonography was used in 13 cases, and the non-navigated ultrasound technology in the remaining 16 cases. Ultrasound scans and videos as well as intraoperative screen shots were saved digitally and evaluated retrospectively, considering image quality, tumor demarcation, orientation, and whether anatomical landmarks were easily visualized. Image-guided scans were compared with non-navigated ultrasound images. Particularly, the green overlay display of the ultrasound scans with a preoperative MRI data set was considered to be helpful for defining the tumor size when the sonographic image suggested either a more sizable tumor or failed to show a clear tumor boundary. This was confirmed by 5 of 5 board certified Neurosurgeons in our department.

Orientation was declared difficult and challenging in 50% of the cases where conventional ultrasound was used. All five board certified Neurosurgeons favoured navigated ultrasound for better orientation and judged it to be superior to non-navigated ultrasound. Especially the orientation of navigated duplex sonography is faster and better to understand compared with non navigated duplex sonography as described technically in article 1.

In summary, this study demonstrated possible advantages of image-guided ultrasound over conventional intraoperative ultrasound through retrospective analysis. However, ultrasound is a real-time imaging technique and should therefore be evaluated live during the examination. A retrospective analysis of stored images and ultrasound videos shows only a selected part of the exam and the interpretation is more difficult, since a certain amount of information was not used.

High frequency Ultrasound

Article 4: Intraoperative ultrasound assistance in the treatment of intradural spinal tumors.

Intraoperative ultrasound has also been used frequently in neurosurgical spinal cases. Regelsberger et al. [2000 and 2005] demonstrated its use for minimizing the spinal opening as well as localizing the tumor intradurally. Our presented series had the goal to evaluate intraoperative ultrasound in visualizing intradural spinal tumors and to assess its potential to improve surgical precision and minimize surgical trauma.

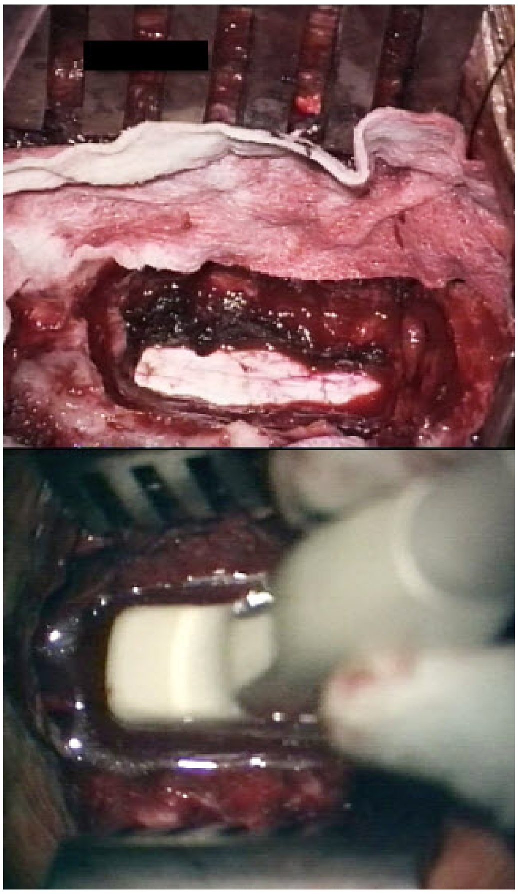
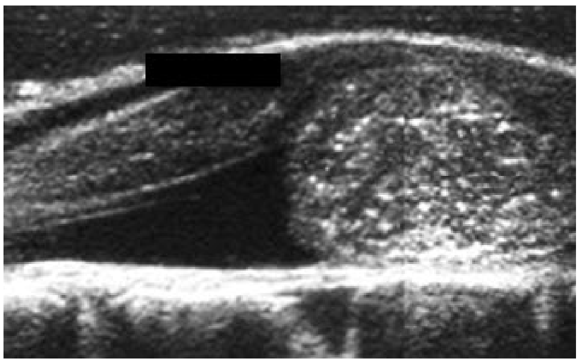


Figure 3: The shape of the linear probe was hockey-stick like (bottom left) and fitted perfectly into small openings like a hemilaminectomy (top left). This way, the minimal invasive opening did not have to be enlarged just for desired imaging. These linear ultrasound probes work in a high-frequency range (7-14 MHz) and deliver high resolution in near field imaging (image below).



In this case series 30 patients with different types of spinal tumors were operated with the aid of high-frequency linear intraoperative ultrasound. Extra- (14) and intramedullary (16) lesions were treated surgically and in 13 cases the procedure was performed by a hemilaminectomy only, the most minimal invasive approach for spinal tumor excision so far. Intraoperative ultrasound altered the surgical approach and laminotomy in 5 cases to reach the tip of the lesion, in order to adapt the approach appropriately according to lesion size before dura opening.

Intramedullary tumors characteristically presented with a heterogenous morphology, sometimes carrying intralesional or perilesional cysts as well as perifocal edema, therefore tumor margins were sometimes poorly defined. This technical setting with its resolution has improved intraoperative spinal imaging, but it is not yet feasible in all heterogenic cavernoma cases for resection control. However, guidance of myelotomy was another important step in spinal tumor surgery and high-frequency linear probes improved this significantly.

Furthermore, image quality may decrease with ongoing resection and one needs to bear in mind that current imaging techniques may not fully reflect the biological extent of the tumor. Currently there is no significant alternative to spinal/dural intraoperative imaging than ultrasound. Intraoperative MRI or CT cannot reach high sufficient or comparable images for intramedullary lesions.

Article 5: Intra-operative high frequency ultrasound improves surgery of intramedullary cavernous malformations.

Based on the previous article and experience, we performed a series of 35 consecutive intradural tumor surgeries in Zurich. We used a newer linear probe which has the same hockey stick form and originates from the Dermatology diagnostics. The frequency range goes here up to 15MHz. In addition we used a new true real time 3D transducer (both Phillips iU22 ultrasound system) to show the difference in resolution and advantages and disadvantages in orientation.

We focused in this study on six special cases with deep intramedullary cavernous malformations that were not visible on the medullary surface even after dura opening. Intraoperative ultrasound images were performed before, during and after the intramedullary cavernoma resection to evaluate once again the possibility of resection control. Complete resection with improved clinical outcome was achieved in all cases. High-frequency intraoperative ultrasound confirmed its value for localization and resolution with further improvement. Resection control was excellent in 3 cases (Fig. 4) and difficult in the other 3 cases due to perifocal edema and hemosiderin infiltration of the myelon.

When using the new true real time 3D probe advantages were only seen in the simultaneously displayed 90° image without moving the probe (which is necessary with the liner probe) (Fig. 4). The resolution decrease from high frequency intraoperative ultrasound (a–c) to real time 3D imaging (d–f) was so significant that resection control with real time 3D intraoperative ultrasound was dropped.

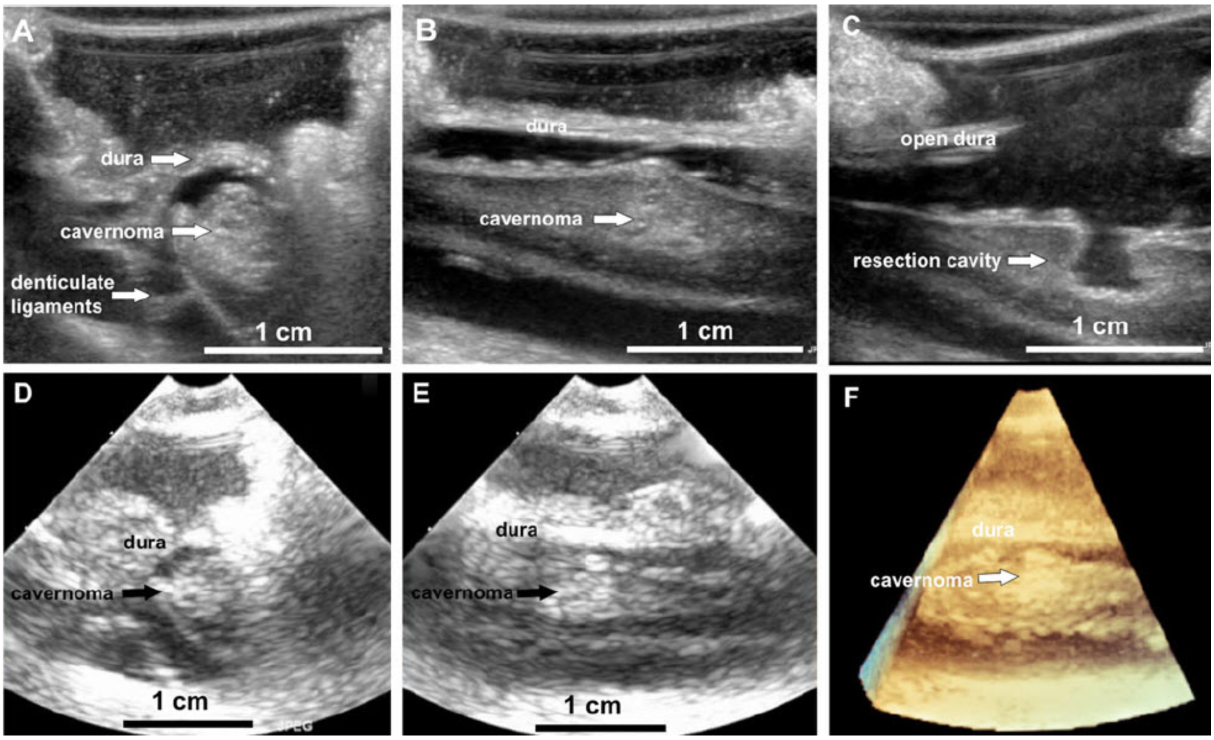


Figure 4: Comparison of the two transducer types (high frequency transducer vs. real time 3D probe). A–C 2D images with the high frequency probe. D–F Images produced by the real time 3D probe. D The corresponding anatomical alignment (cornal image) image to A, and E to B (sagittal plane).F A cone picture from the use of the "live 3D" full volume mode.

The presented high frequency intraoperative ultrasound may have the potential to improve resection control intra-operatively for any intramedullary lesion, since imaging of the lesion and surrounded tissue improved significantly. In our series the resection control was dependent on the active state of the lesion in this series. High frequency intraoperative ultrasound is very well suitable for intraoperative resection control of intramedullary cavernous malformations with little edema surroundings and non-recent bleeding history. However, it needs to be noted that acute lesions do not go necessarily along with perifocal edema. Other circumstances such as venous thrombosis or congestion in acute as well as chronic cavernomas may be associated with perifocal edema. Overall the use of high frequency intraoperative ultrasound showed significantly higher definition compared to usual ultrasound probes (up to 9 MHz) and therefore clear improvement.

Real time-3D Ultrasound

Article 6: Intraoperative localization of intracranial cavernomas by real time 3D ultrasound: First experiences (Technical Note).

Analogue to the previous article, our group used new real time 3D ultrasound also in intracranial cavernomas. These first experiences were published by our visiting doctor under my supervision. The new concept behind true real time 3D imaging is that the array probe allows the acquisition and rendering of full volume data at true real-time frame rates with unparalleled isovoxel resolution. An acquisition procedure is not necessary, as the 3D data are immediately available (live). In the “X-Plane” mode, two ultrasound images are displayed. The left one always shows the 2D ultrasound image according to the position of the probe (oblique). The right one displays the corresponding live 2D image according to the chosen degree of turn (from 0° to 360°) (Article 5, Fig. 4, D and E). The “Live 3D” mode displays all of the ultrasound information from the array probe at once in a cone (Article 5, Fig. 4, F).

This double live imaging improves the quick orientation in cranial surgery, especially if neuronavigation is missing. True real time 3D ultrasound is not yet connected to a navigation system but would represent a next step. However, this array technology utilising 2400 fully sampled elements delivers only medium resolution intraoperatively (2-7 MHz frequency). Further limitations in this preliminary small series were the improper positioning of the patient for intraoperative ultrasound usage (for example sitting position). Especially deep-seated brainstem cavernomas could only be detected with fair image quality and resection control was not performed then.

Nevertheless, this is a newly developed technique in Neurosurgery, with relatively few cases and the technique needs further evaluation concerning its limitations and possibilities.

Article 7: Resection of pediatric intracerebral tumors with the aid of intra-operative real-time 3-D ultrasound

In pediatric neurosurgery, the outcome of surgery often relies on the extension of tumor removal and intraoperative ultrasound offers a radiation-free and safe imaging method. So far, only studies with real time 2D imaging or reconstructed (time-delayed) 3D imaging have been conducted [El Beltagy et al. 2010, Jödicke et al. 1998 and 2004, Unsgaard et al. 2006]. To evaluate the advantages and clinical impact of real time 3D intraoperative ultrasound, we investigated recently a consecutive case series of pediatric brain tumor surgeries operated under the aid of this real time 3D device described in article 6 and 7.

Twenty-two pediatric patients presenting with supra- or infratentorial brain lesions consecutively underwent surgery performed between June 2009 and May 2011 at our Department. The lesions included pilocytic astrocytomas, 5 medulloblastomas, 2 atypical teratoid/rhabdoid tumors, 2 glioblastomas, and 8 other lesions. The ultrasound probe X7-2 was used to acquire real-time 3-D images in combination with the iU22 ultrasound system (Philips, Bothell, USA).

Gross total resection (GTR) was achieved in 18 out of 22 cases (81.8%). In three cases radical resection was avoided, because of infiltration of eloquent structures. Only in one case complete resection was determined by the surgeon, but not confirmed by the neuroradiologist (Fig. 5). A residual tumor was detected and resected in a second surgery one week after the primary surgery. Excluding the 3 intended subtotal resections (STR), the GTR rate was 94.7% (1 out of 19). With regard to the localization of the lesions, almost the same GTR rate of 90% (1 out of 10) was detected for all posterior fossa tumors. There was no permanent neurological deficit in any case due to GTR. Only temporary gait disturbance in most of the posterior fossa cases and limited instances of hormonal dysfunction in suprasellar tumor surgery were noted.

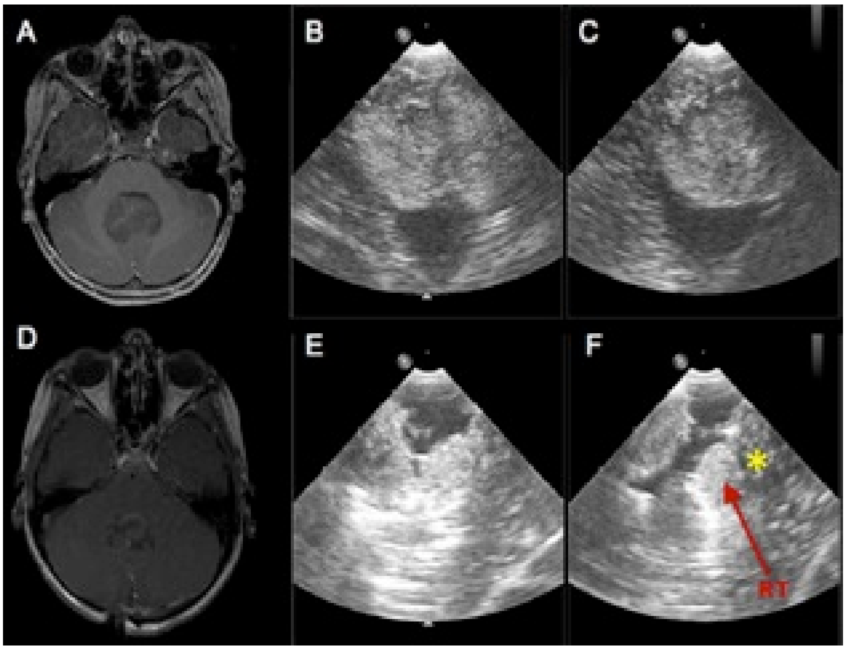


Figure 5: Preoperative axial T1 MRI with contrast (A) of a 9-year old female with a medulloblastoma in the 4^{th} ventricle and the corresponding "X-Plane" 3D IOUS images in "X- Plane" mode as shown in coronar (B) and sagittal (C) planes before tumor removal. Total removal was intended by the surgeon but was not confirmed by the neuroradiologist. On the post-operative axial T1 MRI with contrast (D), a small residual was seen (left to the asterisk) corresponding to the IOUS in coronar (E) and sagittal (F) planes. RT Residual tumor

Especially the removal of cystic or multicystic lesions beneits from intraoperative ultrasound use and in these cases from real time 3D imaging regarding orientation (Fig. 6), similar to the cases published earlier and described in article 2.

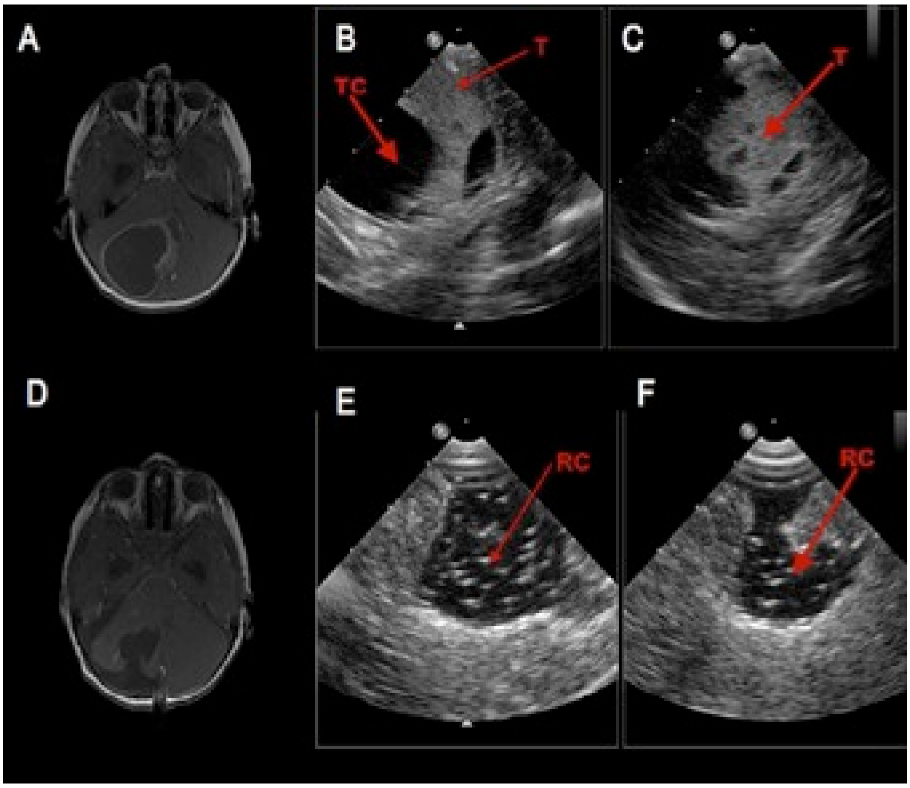
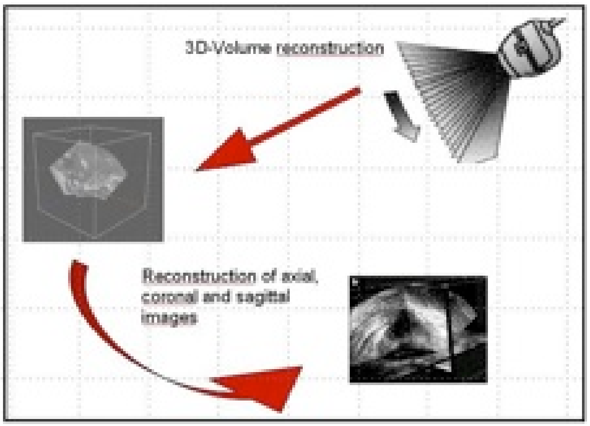


Figure 6: Preoperative axial T1 MRI with contrast (A) of a 4-year old male patient with a pilocytic astrocytoma in the right cerebellum and the corresponding intra-operative rt-3D IOUS images (B, C) in "X- Plane" mode as shown in the coronar (B) and sagittal (C) planes before tumor removal. Rt-3D IOUS of the coronar (E) and sagittal (F) planes and post-operative axial T1 MRI with contrast after 24 hours (D) confirm total removal of the lesion. TC Tumor cyst, T Tumor, RC Resection cavity

Kremer et al. [2006] have reported a GTR rate of 83% when intraoperative MRI was used as a tumor resection control in a study of 35 children. We achieved a GTR rate of 82% overall and 95% in intended GTR in a smaller cohort of 22 pediatric patients using the intraoperative real time 3D ultrasound technique. We achieved fast and real-time imaging of the progress of the operation during all stages of the updated operation. The resolution of our real-time 3-D probe was comparable to standard quality associated with commonly used 2-D ultrasound systems and offered the surgeon enough accuracy to compensate for brain shift. The tip of the real time 3D probe is approximately 3 x 2 cm in size and does not exceed even a minimal craniotomy.

Article 8: Advantages and limitations of intraoperative 3D ultrasound in neurosurgery. Technical note.

There are several ways of intraoperative 3D ultrasound imaging. The most common is the one provided by almost every ultrasound company. Either in an automatic sweep or by movement of the probe in situ by the ultrasound user, a 3D volume is acquired, calculated and displayed on the screen (Fig. 7, left and rightd). This acquisition procedure takes some time (nowadays seconds) and allows only a retrospective view. In cooperation with Brainlab, this technical advancement was incorporated into the IGSonic system and used in over 60 cases in Marburg and partially in Zürich.



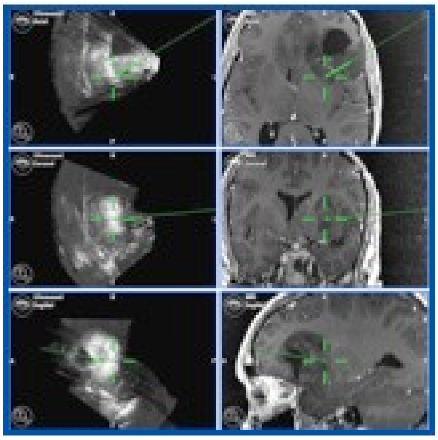


Figure 7: (left) The Navigated 3D ultrasound combines acquired 3D volumes with the preoperative MRI/CT data sets and displays ultrasound images in familiar planes (axial, coronar, sagittal) (Fig. 7 left) next to their corresponding MRI images (Fig. 7 right).

As previously discussed in article 1, intraoperative landmarking of anatomical structures (e.g., vessels or tumor remnants) by ultrasound is still possible and may be fused to intraoperative 3D ultrasound reconstructions. Three-dimensional acquisition in the Doppler mode stores only colour-coded Doppler information, which in summary will reconstruct a 3D vessel superimposed on the navigation images of choice (Fig. 8). Eventually, this can lead to intraoperative non-invasive angiography with further technical support, especially regarding surface-rendering programming.

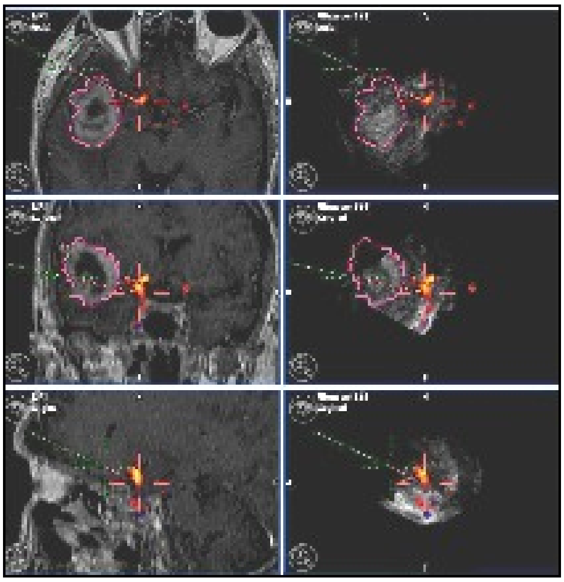


Figure 8: The preoperatively outlined tumor (malignant glioma left temporal lobe) is displayed by intraoperatively ultrasound 3D reconstruction in the familiar planes and though 3D acquisition of the Doppler mode major vessels are landmarked and superimposed (coloured) on both image data sets.

The navigated 3D ultrasound reconstruction has improved orientation furthermore compared to just navigation of 2D images. Unsgaard et al. [2006] have described a similar system and with actually less degradation of resolution compared to the BrainLab version. Additionally the acquisition time is shorter. However, imaging in the familiar planes of axial, coronar and sagittal are possible only retrospectively in both systems, but not live. Live imaging is only possible with 2D ultrasound imaging.

One interesting possibility to use for these navigated 3D ultrasound systems is the standalone procedure. Sufficient imaging of the intended lesion (e.g. cavernoma) by ultrasound can make preoperative MRI/CT image acquisition replaceable. It would offer an intraoperative imaging system in familiar planes with practically no running costs. This could be interesting for settings with limited resources as a true alternative to intraoperative MRI or CT.

The third possibility of intraoperative 3D ultrasound imaging is the true real-time 3D array probe, currently only provided by Philips (X7-2, 2-7 MHz frequency). It is predominantly designed for paediatric cardiologists or gynaecologists. The xMATRIX array technology utilises 2400 fully sampled elements for 360-degree focusing and steering. The array probe enables live xPlane imaging to acquire two full-resolution planes simultaneously from the same heartbeat or region of interest. The system's multi-directional beam steering provides unlimited planes in all directions, and live volume imaging allows the acquisition and rendering of full volume data at true real-time frame rates with unparalleled isovoxel resolution. The settings on the system are not primarily ordered for neurosurgical procedures, according to the company. However, there is increasing corporate interest in further adapting parameters for brain and tumor visualisation, which is crucial for optimal ultrasound imaging. The real-time 3D ultrasound system itself (with additional transducers) is a high-end, modern intraoperative imaging device with minimal running costs.

In summary, 3D intraoperative ultrasound improves significantly orientation, whether through combination with navigation or by real time imaging. However, image quality or resolution are not equal to high end 2D probes in higher frequency range.

Outlook and future

Intraoperative 3D ultrasound

Navigated 3D ultrasound has the disadvantage of required acquisition time. Real time 3D images cannot be displayed yet in the familiar planes of axial, coronar and sagittal. A connection of real time 3D probes to a navigation system and immediate fast calculation of the tracked 3D volume data would produce an excellent live (!) intraoperative imaging modality in the familiar planes. (Fig. 9) We are currently working with BrainLab and Philips on such a system combination.

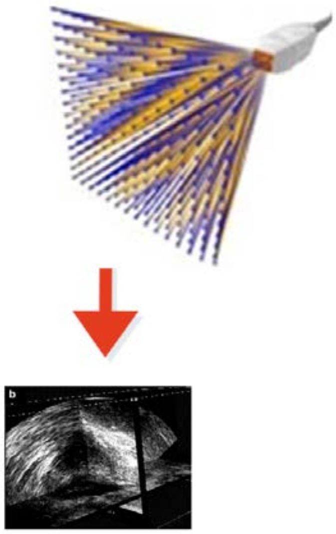


Figure 9: The 3D beam from real time ultrasound probes should be converted immediately to an axial, coronal and sagittal view to simplify orientation for the surgeon.

Our experience with real time-3-D intraoperative ultrasound use for pediatric patients is encouraging, but we are not yet satisfied with the image resolution. There is no doubt that this technique will improve. A new probe with 9600 arrays (but lower frequency breadth) has been recently released and is currently under evaluation at our Department. The image size will increase and “CT-like” images can be achieved, but resolution in near field area will not benefit from this.

High frequency intraoperative ultrasound

Based on the good experience with high frequency linear probes in spinal surgery, we started to use this probe for intracranial surgery. It changes dogmatically the way of image acquisition. The way to acquire ultrasound images of the brain is extra- or intradurally, but most likely outside the resection cavity to receive an image of the complete resection hole (Fig. 10 A). With the small hockey stick probe and excellent imaging in near field range (Fig. 11), one must go closer to the surface of the initial tumor boarder and acquire partial fields for resection control (Fig. 10 B).

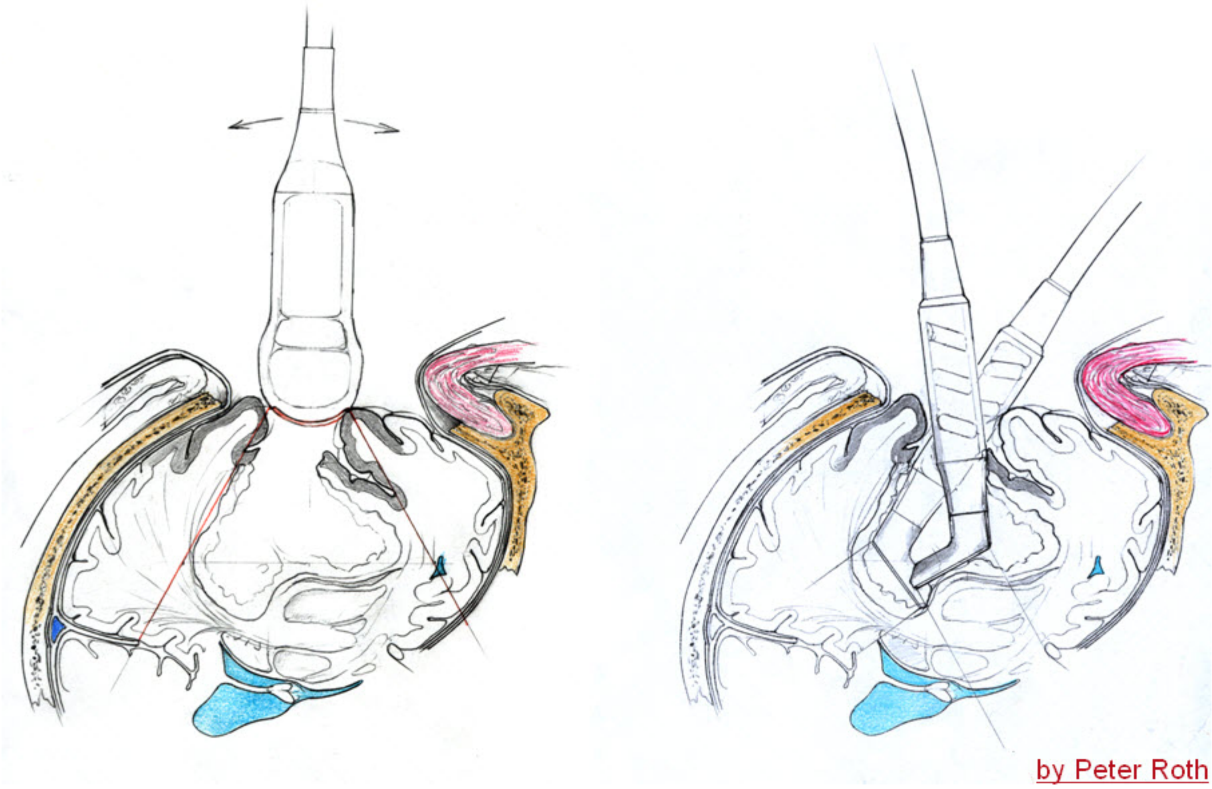


Figure 10: Image A (left) shows the conventional intraoperative ultrasound use. The probe is held outside the resection cavity, which is filled with saline. The aquired images give an overview of the resection cavity. In distant areas residual tumor is sometimes difficult to differentiate from blood or edema. Image B (right) demonstrates the closer scanning of the resection cavity surface. Here the first 10 mm are or importance and differentiation of structures is better.

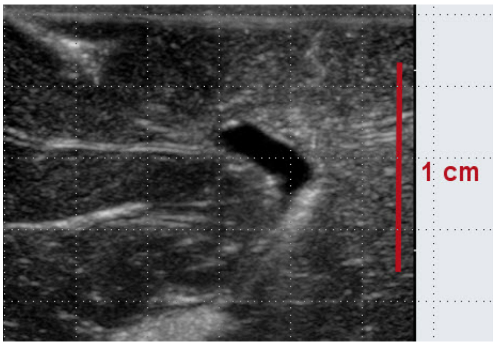


Figure 11: Images of detailed anatomical structuring are possible and definitely improve the highly appreciated resolution in cerebral surgery demonstrating the amygdala/hippocampus in near field ultrasound through the resection cavity as shown in Fig. 10 B.

We operated with this technique over the last 2 years and submitted our clinical outcome data in a consecutive case series of intracranial tumors with very promising results (GTR over 95%) (Fig 12). Currently, we plan a prospective study comparing different intraoperative imaging modalities (such as iMRI, fluorescence guidance (5-aminolevulinic acid) and ultrasound). This high frequency probe (up to 15 MHz) finally gives a chance to compete with high field intraoperative MRI imaging. A combination with neuronavigation would be highly appreciated for better orientation, but the movement of the probe is basically 360° and will be very difficult to track it constantly. A 360° tracking device is not yet on the market.

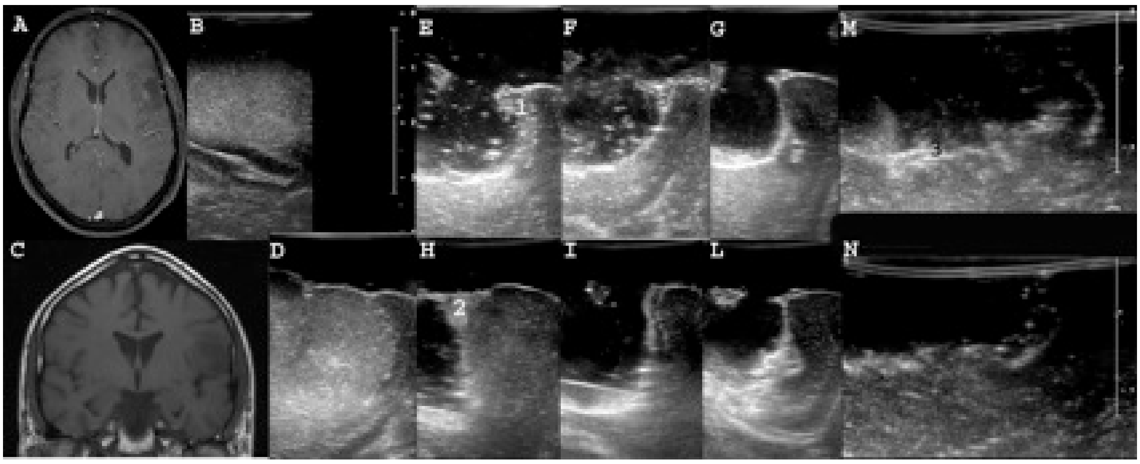


Figure 12: Preoperative MR scan (A and C) and transdural high frequency intraoperative ultrasound (B and D) of an opercular left anaplastic astrocytoma. Figure E,F,G and H,I,L illustrate the sequential resection of two different tumor remnants (1 and 2) at the cavity's margins. In M the probe was introduced in the cavity. The closer scanning of the walls at the end of macroscopic total resection showed a suspicious hyperechogenic area (3), which was then further removed (N).

Conclusion

Intraoperative real time 3-D ultrasound improves the orientation for an experienced ultrasound user by simultaneous display of two images in the degree of choice. Inexperienced ultrasound users should make use of ultrasound and neuronavigation combined systems. Improvements in resolution can only be achieved by higher frequency ranges, which will change the general understanding of intraoperative ultrasound usage and image interpretation. The usual broad exposure will most likely change to superficial imaging. However, this increase in detailed imaging can push intraoperative ultrasound further to a high quality intraoperative imaging alternative.

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